(12) UK Patent Application (19) GB (11) 2 230 190 (13) A

(43) Date of A publication 17.10.1990

(21) Application No 8906947.0

(22) Date of filing 28.03.1989

(71) Applicant
Imperial Chemical Industries Plc

(Incorporated in the United Kingdom)

Imperial Chemical House, Millbank, London, SW1P 3JF, United Kingdom

(72) Inventor
Fraser Forrest Morpeth

(74) Agent and/or Address for Service
David Gomer James
Imperial Chemical Industries Plc, Legal Department Patents, P O Box No.6, Bessemer Road, Welwyn Garden City, United Kingdom

(51) INT CL[5]
A01N 43/80 59/16 // (A01N 43/80 43.40) (A01N 59/16 43:40 43:80)

(52) UK CL (Edition K)
A5E EBB E105 E115 E246 E251 E258 E260 E264 E271 E272 E273
U1S S1275 S1276 S1289 S1293 S1364 S1391 S1407 S1434 S1457 S1529 S1612

(56) Documents cited
None

(58) Field of search
UK CL (Edition J) **A5E EBB**
INT CL[4] **A01N 43/80 59/00**
Online databases: CAS ONLINE

(54) **Compositions containing an isothiazolin(thi)one derivative and a 2-mercaptopyridine-1-oxide derivative**

(57) A composition contains an isothiazolinone or an isothiazolothione derivative and either an alkali metal salt of 2-mercaptopyridine-1-oxide or a metal salt together with 2, 2'-dithiopyridine-1,1'-dioxide. The isothiazolinone derivative can be 1, 2-benzisothiazolin-3-one or a metal salt or complex thereof. The salt of 2-mercaptopyridine-1-oxide may be a sodium salt and the salt used together with 2, 2'-dithiopyridine-1,1'-dioxide may be zinc chloride. The compositions have *antimicrobial* properties and are effective against a range of bacteria and fungi.

GB 2 230 190 A

COMPOSITION, PRODUCTION AND USE

The present invention relates to compositions which are useful as industrial biocides.

Industrial biocides are useful to prevent industrial spoilage, in particular that caused by bacteria and fungi. Industrial biocides find application in the preservation of paints, latices, adhesives, leather, wood, metal working fluids and cooling water.

One class of compound which can be used as an industrial biocide is based on the isothiazolinone structure. There are many disclosures of isothiazolinone derivatives which are stated to have useful biocidal properties. US Patent 3761488 discloses isothiazolinone derivatives in which alkyl, alkenyl, alkynyl, cycloalkyl, aralkyl or aryl groups, which may optionally be substituted, are attached to the nitrogen atom and the 4 and 5 positions are unsubstituted or are substituted with halogen or lower alkyl groups. US Patent 3517022 discloses benzisothiazolones in which a carbamoyl group is attached to the nitrogen atom and the benzene ring may be optionally substituted. US Patent 3950349 discloses N-thio-substituted isothiazolin-3-one compounds which may be isothiazolone or benzisothiazolone derivatives. US Patent 4165318 discloses a solution of a 3-isothiazolone in a polar organic solvent, wherein the solution also contains a stabilising amount of formaldehyde. British Patent Specification 2087388 discloses 4,5-polymethylene-4-isothiazoline-3-one in which the polymethylene chain has three or four carbon atoms.

Another class of compound which is stated to be fungicidal is based on the isothiazolothione structure. British Patent Specification 1113634 discloses compounds of this type or an isomeric form thereof, in which the 4 and 5 positions are unsubstituted or may be substituted with alkyl or aryl groups or which may form a part of a further ring system.

Isothiazolin-3-ones which are unsubstituted on the nitrogen atom are capable of forming salts for example with alkali metal such

as sodium and potassium, and with ammonia or amines such as triethanolamine. These salts are generally water-soluble. British Patent Specification 1191253 describes and claims high strength aqueous solutions of crude 1,2-benzisothiazolin-3-one in the form of a mixture of two or more different amine salts thereof, the amines being selected from diethanolamine, triethanolamine, diisopropanol amine, triisopropanolamine and morpholine. British Patent Specification 1330531 discloses compositions of 1,2-benziso-thiazolin-3-one in aliphatic, cycloaliphatic or heterocyclic amines which contain 2 to 6 carbon atoms and which are free from hydroxyl and ether groups. British Patent Specification 2004747 discloses solutions of an alkali metal salt of 1,2-benzisothiazolin-3-one in a hydroxylic organic solvent such as propylene glycol, dipropylene glycol and polyethylene glycols.

However such salt solutions require the addition of considerable quantities of extra organic solvent, for example glycols, to be stable enough to be commercially acceptable.

Compounds and compositions of the foregoing types, and related compounds of the same general type, are effective to a varying degree, depending on the particular compound or composition, against a range of bacteria and/or fungi. However, to reduce the cost of using these compounds it is desirable to improve their effectiveness as antimicrobial materials.

Compositions have been proposed which contain more than one compound which has antimicrobial properties. In general such compositions show an aggregate of the properties of the compounds present in the composition. Typically such compositions contain one compound which exhibits useful antibacterial properties together with a different compound which exhibits useful antifungal properties.

We have now found that certain compositions possess surprisingly useful antimicrobial properties.

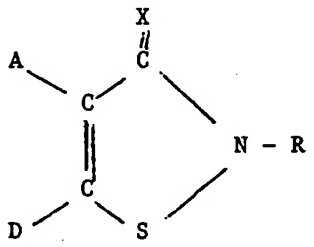
Thus, according to the present invention there is provided a composition which comprises

(a) at least one isothiazolinone derivative or at least one isothiazolothione derivative, and

(b)(i) an alkali metal salt of 2-mercaptopyridine-1-oxide; or

(b)(ii) a mixture of 2,2'-dithiopyridine-1,1'-dioxide together with a salt of a metal.

The isothiazolinone or isothiazolothione derivative which is component (a) of the composition is typically a compound of the general formula:



wherein:

X is an oxygen or sulphur atom;

R is a hydrogen atom, a substituted or unsubstituted hydrocarbyl group, a substituted or unsubstituted hydrocarbylthio group, a substituted or unsubstituted hydrocarbyloxy group, a carbamoyl group or a cation;

A is a hydrogen atom, a halogen atom, a cyano group, or a substituted or unsubstituted hydrocarbyl group;

D is a hydrogen atom, a halogen atom, a cyano group, or a substituted or unsubstituted hydrocarbyl group; or

A and D, together with the carbon atoms to which they are attached, form a five- or six-membered ring, which may optionally be substituted.

Preferably component (a) is at least one isothiazolinone derivative, that is a compound in which X is an oxygen atom. If the groups R, A and D are, or contain, substituted hydrocarbyl groups, the substituents are typically halogen, alkoxy or alkylthio, particularly those in which the alkyl groups contain 1 to 4 carbon

atoms. If R is a carbamoyl group, this is of the general type $-CONHR^1$ where R^1 is a hydrogen atom or a hydrocarbyl group, which may be substituted. It is generally preferred that the group R is a hydrogen atom or a lower alkyl group, that is an alkyl group containing 1 to 4 carbon atoms. R is especially hydrogen or a methyl group.

A and D may, together with the carbon atoms to which they are attached, form a five- or six-membered ring, which may be substituted, the substituents typically being halogen, alkyl, alkoxy or alkylthio groups. The ring thus obtained may contain a heteroatom, for example a nitrogen atom but in general A and D form a hydrocarbon ring such as a benzene, cyclopentene or cyclohexene ring. Alternatively, A and D are separate groups and one or both of A and D can be a hydrogen atom. It is generally preferred that at least one of A and D is other than a hydrogen atom and is, particularly, a halogen atom, for example chlorine or a lower alkyl group.

Compounds which can be used as component (a) of the mixture include 5-chloro-2-methylisothiazolin-3-one (R is methyl, A is hydrogen and D is chlorine); 4,5-dichloro-2-methylisothiazolin-3-one (R is methyl and A and D are both chlorine); 1,2-benziso-thiazolin-3-one (R is hydrogen and A and D, together with the carbon atoms to which they are attached, form a benzene ring); 4,5-trimethylene-4-isothiazolin-3-one (R is hydrogen and A and D, together with the carbon atoms to which they are attached, form a cyclopentene ring); and 2-methyl-4,5-trimethylene-4-isothiazolin-3-one (R is methyl and A and D, together with the carbon atoms to which they are attached, form a cyclopentene ring).

In component (a), if R is a cation this may be a cation having a valency of more than one but is particularly a monovalent cation such as an alkali metal, an amine or quaternary ammonium cation. As noted previously herein, such materials are generally water-soluble and hence can be used in an aqueous medium.

The other component of the mixture may be an alkali metal salt of 2-mercaptopyridine-1-oxide. The alkali metal is conveniently sodium.

The alkali metal salt may be prepared by the reaction of a compound of the alkali metal, for example an oxide, hydroxide, carbonate, or bicarbonate, with 2-mercaptopyridine-1-oxide. The reaction is preferably carried out in a liquid medium in which the compound of the alkali metal is soluble. Preferably the liquid medium is one in which 2-mercaptopyridine-1-oxide is also soluble. Suitable liquids which may be used include water and lower alcohols, that is alcohols containing not more than 4 carbon atoms, especially methanol or ethanol. The reaction is conveniently effected by the addition of 2-mercaptopyridine-1-oxide to a solution of a compound of the alkali metal in a suitable solvent. The 2-mercaptopyridine-1-oxide is preferably added in an essentially stoichiometric amount. The alkali metal salt obtained may be soluble in the liquid medium or may be insoluble and separate as a precipitate. An insoluble salt may be separated from the liquid reaction medium by known techniques such as filtration or removing a supernatant liquid. The salt may be washed with a suitable liquid medium such as that in which the salt was prepared. If the alkali metal salt is soluble in the reaction medium, it may be used as prepared without being separated from the reaction mixture. Alternatively the metal salt may be separated and, if necessary, purified using known techniques such as evaporating the solution to dryness and purifying, as necessary, by one or more crystallisations using a suitable solvent.

The compound of the alkali metal is conveniently an oxide, hydroxide, carbonate or bicarbonate. Reaction of the appropriate alkali metal hydroxide with 2-mercaptopyridine-1-oxide is an especially convenient method of preparing the desired salt. The alkali metal salt is soluble in water and remains in solution if prepared in an aqueous medium. The aqueous solution of the alkali metal salt may be used as obtained or the alkali metal salt may be separated and purified by conventional procedures. The sodium salt of 2-mercaptopyridine-1-oxide is commercially available and component (b)(i) is conveniently the sodium salt.

The other component of the mixture may be a mixture of 2,2'-dithiopyridine-1,1'-dioxide together with a salt of a metal. The metal may be a metal of Groups IA to VA or IB to VIIB of the Periodic Table. All references herein to the Periodic Table are to the Periodic Table according to Mendeleoff, as set out on the inside rear cover of "Handbook of Chemistry and Physics" 49th Edition (1968-1969) published by the Chemical Rubber Co., Cleveland, Ohio, USA.

The salt of a metal is suitably a salt of an alkali metal, conveniently sodium, or a salt of a divalent metal, for example a metal of Group IIB such as zinc. Any suitable metal salt may be used, for example a metal halide, and it is preferred that the metal salt is one which is soluble to the extent of at least 1% w/v in water. The relative proportions of metal salt and 2,2'-dithiopyridine-1,1'-dioxide may be varied but are preferably in essentially stoichiometric amounts, that is for each mole of 2,2'-dithiopyridine-1,1'-dioxide there is used 2/n moles of the metal salt, where n is the valency of the metal in the salt.

We have obtained useful compositions by mixing 1,2-benzisothiazolin-3-one with a sodium salt of 2-mercaptopyridine-1-oxide or with a mixture of zinc chloride and 2,2'-dithiopyridine-1,1'-dioxide.

In subsequent references to the compositions of the present invention, "component (b)" is used to include (b)(i), (b)(ii) and mixtures thereof.

The relative proportions of the components of the composition can vary and compositions having useful properties can be obtained which contain from one part by weight of component (a) or component (b) and correspondingly up to 1000 parts by weight of component (b) or component (a). The preferred proportions are dependent on the compounds used as component (a) and component (b), and also the particular system in which the mixture is to be used. In general the composition contains at least 1 part by weight of one component and not more than 100 parts by weight of the other component.

The compositions of the present invention have antimicrobial properties. We have found that compositions in accordance with the present invention are active against both bacteria and fungi. Furthermore, compositions in accordance with the present invention are such that the sum of the fractional inhibitory concentration (FIC) for all the components of the composition is less than one and, with preferred compositions is less than 0.7. Especially preferred compositions are those in which the sum of the FIC for all the components of the composition is not more than 0.5. The FIC is the ratio of the concentration of an individual component to the minimum inhibitory concentration of that component. It will be appreciated that if the value of the sum of the FIC for all the components of the composition is less than one, the composition is synergistic, the extent of synergy being indicated by the amount by which the sum of the FIC is below one. We have found that some compositions in accordance with the present invention are such that the sum of the FIC is less than 0.5 and may be 0.4 or even lower.

The compositions of the present invention have antimicrobial properties and are suitable for use as industrial biocides.

The compositions of the present invention provide good wet state preservation and hence may be used as a cutting fluid preservative and also in cooling water applications. Wood and leather preservation is another field of application of the compositions. The compositions of the present invention can also be incorporated into paint, as paint film fungicide that can be used without addition of a bactericide.

The materials which are component (a) and component (b) of the composition of the present invention are soluble in many polar solvents, although the solubility is dependent on the nature of the particular compounds which are present in the composition. However, many of the compounds are soluble in water, alcohols, ethers, ketones and other polar solvents or mixtures thereof.

The compositions of the present invention may be used alone as an antimicrobial material but may also be used in, or on, a suitable carrier material.

Thus, as a further aspect of the present invention there is provided a biocide composition comprising a carrier and an effective amount of a composition of components (a) and (b) in accordance with the invention.

The carrier is typically a material which shows little, if any, antimicrobial activity and may be, or include, a material which is susceptible to the growth of micro-organisms, particularly fungi. The carrier is preferably a liquid medium and the biocide composition may be a solution, suspension or emulsion of the composition of components (a) and (b) in a liquid carrier. The carrier may be water, in which one or both of components (a) and (b) are essentially insoluble, or may be a liquid such as acetic acid, N,N-dimethyl-formamide, propylene glycol, dimethyl sulphoxide or N-methyl-2-pyrrolidone in which at least one, and preferably both, of components (a) and (b) are soluble. Alternatively, a mixture of liquids may be used, one being a solvent for component (a) and component (b) and the other being a non-solvent for both components, and using such a mixture the composition typically comprises an emulsion or droplets of a solution of components (a) and (b) in the solvent therefor dispersed in the non-solvent. If a suspension or emulsion is used, this conveniently contains a surface active agent which is effective to maintain the non-continuous phase as a suspension or emulsion. Any surface active agent known for use in biocide compositions may be used in such a system, for example alkylene oxide adducts of fatty alcohols, alkyl phenols and amines such as ethylene diamine.

The amount of the composition which is present in the biocide composition may be just sufficient to have an antimicrobial effect or the composition may be present in a substantially greater proportion. It will be appreciated that the biocide composition may be provided as a concentrated solution which is subsequently diluted for use as an antimicrobial material. Thus, the amount of the composition of components (a) and (b) which is present in the biocide composition is typically in the range from 0.0001% up to 10% by weight of the biocide composition.

The composition of the present invention is especially effective in providing anti-bacterial activity. Thus, the compositions can be used for the treatment of various media to inhibit the growth of micro-organisms.

As a further aspect of the present invention there is provided a method for inhibiting the growth of micro-organisms on, or in, a medium which comprises treating the medium with a composition of components (a) and (b) as hereinbefore defined.

The composition can be used in conditions in which micro-organisms grow and cause problems. Systems in which micro-organisms cause problems include liquid, particularly aqueous, systems such as cooling water liquors, metal working fluids, geological drilling lubricants, polymer emulsions and surface coating compositions such as paints, varnishes and lacquers and also solid materials such as wood and leather. The composition of the present invention can be included in such materials to provide an anti-microbial effect. The amount of the composition is typically in the range from 0.0001 up to 10%, preferably 0.0005 up to 5% and especially 0.0005 to 2% by weight of the composition relative to the system to which it is added.

Components (a) and (b) of the composition of the present invention may be the only antimicrobial compounds or may be used together with further compounds having antimicrobial characteristics. The composition may contain more than one compound which is component (a) and/or may contain more than one salt, complex or mixture which is component (b). Alternatively, a composition of components (a) and (b) in accordance with the present invention may be used together with one or more known antimicrobial compounds. The use of a mixture of anti-microbial compounds can provide a composition having a broader anti-microbial spectrum and hence one which is more generally effective than the components thereof. The known antimicrobial may be one possessing anti-bacterial, anti-fungal, anti-algal or other antimicrobial characteristic. The mixture of the composition of the present invention with other

antimicrobial compounds typically contains from 1 to 99% by weight, relative to the weight of total antimicrobially active compounds, of the composition of components (a) and (b), and particularly from 40 to 60% by weight of the composition of components (a) and (b).

As examples of known antimicrobial compounds which may be used, together with the metal complex of the present invention, there may be mentioned quaternary ammonium compounds such as diethyldodecylbenzyl ammonium chloride; dimethyloctadecyl-(dimethylbenzyl)ammonium chloride; dimethyldidecylammonium chloride; dimethyldidodecylammonium chloride; trimethy-tetradecylammonium chloride; benzyldimethyl(C_{12}-C_{18} alkyl)ammonium chloride; dichlorobenzyldimethyldodecylammonium chloride; hexadecylpyridinium chloride; hexadecylpyridinium bromide; hexadecyltrimethylammonium bromide; dodecylpyridinium chloride; dodecylpyridinium bisulphate; benzyldodecyl-bis(beta-hydroxyethyl)ammonium chloride; dodecyl-benzyltrimethylammonium chloride; benzyldimethyl(C_{12}-C_{18} alkyl) ammonium chloride; dodecyldimethylethyl ammonium ethylsulphate; dodecyldimethyl-(1-naphthylmethyl)ammonium chloride; hexadecyl-dimethylbenzyl ammonium chloride; dodecyldimethylbenzyl ammonium chloride and 1-(3-chloroallyl)-3,5,7-triaza-1-azonia-adamantane chloride; urea derivatives such as 1,3-bis(hydroxymethyl)-5,5-dimethylhydantoin; bis(hydroxymethyl)urea; tetrakis(hydroxy-methyl)acetylene diurea; 1-(hydroxymethyl)-5,5-dimethylhydantoin and imidazolidinyl urea; amino compounds such as 1,3-bis(2-ethyl-hexyl)-5-methyl-5-aminohexahydropyrimidine; hexamethylene tetra amine; 1,3-bis(4-aminophenoxy)propane; and 2-[(hydroxymethyl)-amino]ethanol; imidazole derivatives such as 1[2-(2,4-dichloro-phenyl)-2-(2-propenyloxy)ethyl]-1H-imidazole; 2-(methoxycarbonyl-amino)-benzimidazole; nitrile compounds such as 2,4,5,6-tetra-chloroisophthalodinitrile and 1,2-dibromo-2,4-dicyanobutane; thiocyanate derivatives such as methylene bis thiocyanate; tin compounds or complexes such as tributyltin-oxide, chloride, naphthoate, benzoate or 2-hydroxybenzoate; thiazole derivatives such as 2-(thiocyanomethylthio)-benzthiazole; and mercaptobenzthiazole;

nitro compounds such as tris(hydroxymethyl)nitromethane; 5-bromo-5-nitro-1,3-dioxane and 2-bromo-2-nitropropane-1,3-diol; aldehydes and derivatives such as gluteraldehyde (pentanedial) p-chlorophenyl-3-iodopropargyl formaldehyde and glyoxal; amides such as chloracetamide; N,N-bis(hydroxymethyl)chloracetamide; N-hydroxymethyl-chloracetamide and dithio-2,2-bis(benzmethyl amide); guanidine derivatives such as poly hexamethylene biguanide and 1,6-hexamethylene-bis[5-(4-chlorophenyl)biguanide]; thiones such as 3,5-dimethyltetrahydro-1,3,5-2H-thiodiazine-2-thione; triazine derivatives such as hexahydrotriazine and 1,3,5-tri-(hydroxyethyl)-1,3,5-hexahydrotriazine; oxazolidine and derivatives thereof such as bis-oxazolidine; furan and derivatives thereof such as 2,5-dihydro-2,5-dialkoxy-2,5-dialkylfuran; carboxylic acids and the salts and esters thereof such as sorbic acid and the salts thereof and 4-hydroxybenzoic acid and the salts and esters thereof; phenol and derivatives thereof such as 5-chloro-2-(2,4-dichloro-phenoxy)phenol; thio-bis(4-chlorophenol) and 2-phenylphenol; sulphone derivatives such as diiodomethyl-paratolyl sulphone, 2,3,5,6-tetrachloro-4-(methylsulphonyl) pyridine and hexachlorodimethyl sulphone.

Further aspects of the present invention are described in the following illustrative examples.

In the following examples, compositions in accordance with the present invention were subjected to evaluation of the antimicrobial properties of the compositions. The evaluation was effected, under sterile conditions throughout, as follows:

In the microbiological evaluation, various compositions were tested for anti-microbial activity against bacteria. The bacteria used were one or more of Escherichia coli and Staphylococcus aureus.

These test organisms will be referred to hereafter as EC and SA.

Microbiological evaluation

The materials, or mixture of materials, to be tested were added to a nutrient broth in amounts to give a desired concentration of the added material. The added materials were added at concentrations from zero to above the minimum inhibitory concentration of the particular material In the mixtures, the concentrations of each material were varied in a systematic fashion to give a matrix of mixtures of different relative proportions and different total concentrations.

The effect on the inhibition of growth of bacteria was investigated by inoculating each sample of broth with sufficient of the test bacterium to give about 10^5 cells cm^{-3}. The mixture was incubated at 30°C for 48 hours. At the end of the test period the presence of turbidity in the broth indicated that growth of the test bacterium had occurred. A lack of turbidity was indicative that no growth had occurred. The results were used to draw an isobologram from which the sum of the fractional inhibitory concentration for a mixture can be determined.

Example 1

The microbiological evaluation as described was carried out using the bacterium, Escherichia coli. The composition tested was a mixture of 1,2-benzisothiazolin-3-one and sodium 2-thiopyridine-1-oxide.

The concentrations of 1,2-benzisothiazolin-3-one used were 0, 1, 2.5, 5 and 10 microgram cm^{-3}. Sodium 2-thiopyridine-1-oxide was used at concentrations of 0, 250, 500, 750 and 1000 microgram cm^{-3}.

From the results obtained, it was found that the lowest sum of the fractional inhibitory concentration (FIC) was 0.45 which was achieved with a mixture containing 2.5 microgram cm^{-3} of 1,2-benzisothiazolin-3-one and 250 microgram cm^{-3} of sodium 2-thiopyridine-1-oxide. Table One sets out mixtures and the sum of FIC.

Table One

Mixture		FIC
BIT (a) (ppm)	STPO (b) (ppm)	
1	750	0.7
1	1000	0.9
2.5	250	0.45

Notes to Table One

(a) BIT is 1,2-benzisothiazolin-3-one.

(b) STPO is sodium 2-thiopyridine-1-oxide.

Example 2

The procedure of Example 1 was repeated with the exception that the bacterium EC was replaced by the bacterium SA and sodium 2-thiopyridine-1-oxide was used at concentrations of 0, 0.1, 0.5, 1.0 and 2.5 microgram cm^{-3}.

From the results obtained, it was found that the lowest value of FIC was 0.6 which was achieved with a mixture containing 5.0 microgram cm^{-3} of 1,2-benzisothiazolin-3-one and 0.1 microgram cm^{-3} of sodium 2-thiopyridine-1-oxide. Table Two sets out mixtures and the sum of FIC.

Table Two

Mixture		FIC
BIT (a) (ppm)	STPO (b) (ppm)	
5	0.1	0.6
2.5	0.5	0.75

Notes to Table Two

(a) and (b) are as defined in Notes to Table One.

Example 3

The procedure of Example 1 was repeated with the exception that the composition was a mixture of 1,2-benzisothiazolin-3-one, 2,2'-dithiopyridine-1,1'-dioxide and zinc chloride.

The concentrations of 1,2-benzisothiazolin-3-one were as used in Example 1. 2,2'-dithiopyridine-1,1'-dioxide was used at concentrations of 0, 0.5, 1.0, 2.5, 5 and 10 microgram cm^{-3}. Zinc chloride was used at concentrations of 0 and 10 microgram cm^{-3}.

In the absence of 2,2'-dithiopyridine-1,1'-dioxide, control was obtained with a mixture containing 2.5 microgram cm^{-3} of 1,2-benzisothiazolin-3-one and 10 microgram cm^{-3} of zinc chloride. In the presence of 2,2'-dithiopyridine-1,1'-dioxide, control was obtained with a mixture containing 0.5 microgram cm^{-3} of 1,2-benzisothiazolin- 3-one, 10 microgram cm^{-3} of zinc chloride and 1.0 microgram cm^{-3} of 2,2'-dithiopyridine-1,1'-dioxide, corresponding to a sum of FIC of 0.4. Table Three sets out mixtures and the sum of FIC.

Table Three

Mixture			FIC
BIT (a) (ppm)	DTP (c) (ppm)	ZC (d) (ppm)	
0.5	1.0	10	0.4
0.5	2.5	10	0.7
1.0	1.0	10	0.6

Notes to Table Three

(a) is as defined in Notes to Table One.

(c) DTP is 2,2'-dithiopyridine-1,1'-dioxide.

(d) ZC is zinc chloride.

CLAIMS

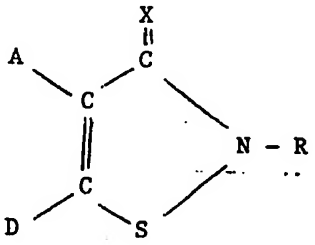
1. A composition which comprises

(a) at least one isothiazolinone derivative or at least one isothiazolothione derivative, and

(b)(i) an alkali metal salt of 2-mercaptopyridine-1-oxide; or

(b)(ii) a mixture of 2,2'-dithiopyridine-1,1'-dioxide together with a salt of a metal.

2. A composition as claimed in claim 1 wherein (a) is at least one compound of the general formula:



wherein:

X is an oxygen or sulphur atom;

R is a hydrogen atom, a substituted or unsubstituted hydrocarbyl group, a substituted or unsubstituted hydrocarbylthio group, a substituted or unsubstituted hydrocarbyloxy group, a carbamoyl group or a cation;

A is a hydrogen atom, a halogen atom, a cyano group, or a substituted or unsubstituted hydrocarbyl group;

D is a hydrogen atom, a halogen atom, a cyano group, or a substituted or unsubstituted hydrocarbyl group; or

A and D, together with the carbon atoms to which they are attached, form a five- or six-membered ring, which may be substituted.

3. A composition as claimed in claim 2 wherein in component (a) X is an oxygen atom.

4. A composition as claimed in either claim 2 or claim 3 wherein R is a carbamoyl group of the type $-CONHR^1$, wherein R^1 is a hydrogen atom or a substituted or unsubstituted hydrocarbyl group.

5. A composition as claimed in either claim 2 or claim 3 wherein R is a hydrogen atom or an alkyl group containing 1 to 4 carbon atoms.

6. A composition as claimed in any one of claims 2 to 5 wherein A and D together with the carbon atoms to which they are attached, form a substituted or unsubstituted five- or six-membered hydrocarbon ring.

7. A composition as claimed in any one of claims 2 to 5 wherein one of the groups A and D is a halogen atom or an alkyl group containing 1 to 4 carbon atoms and the other of the groups A and D is a hydrogen atom, a halogen atom or an alkyl group containing 1 to 4 carbon atoms.

8. A composition as claimed in any one of claims 2, 3 and 5 to 7 in which component (a) is selected from 5-chloro-2-methylisothiazolin-3-one; 4,5-dichloro-2-methylisothiazolin-3-one; 1,2-benzisothiazolin-3-one; 4,5-trimethylene-4-isothiazolin-3-one and 2-methyl-4,5-trimethylene-4-isothiazolin-3-one.

9. A composition as claimed in claim 5 wherein R is a cation which is a monovalent cation selected from an alkali metal, an amine or a quaternary ammonium.

10. A composition as claimed in any one of claims 1 to 9 wherein (b)(i) is the sodium salt of 2-mercaptopyridine-1-oxide.

11. A composition as claimed in any one of claims 1 to 9 wherein the metal present in the salt of a metal in the mixture of (b)(ii) is a metal of Group IA to VA or IB to VIIB.

12. A composition as claimed in claim 11 wherein the metal is an alkali metal or zinc.

13. A composition as claimed in claim 12 wherein (b)(ii) is a mixture of 2,2'-dithiopyridine-1,1'-dioxide and zinc chloride.

14. A composition as claimed in any one of claims 1 to 13 which contains from one part by weight of (a) or of component (b)(i) or component (b)(ii) or mixture of (b)(i) and (b)(ii) and correspondingly up to 1000 parts by weight of component (b)(i) or component (b)(ii) or mixture of (b)(i) and (b)(ii) or of component (a).

15. A composition as claimed in claim 14 which contains at least one part by weight of one component, or mixture of components, and not more than 100 parts by weight of the other component or mixture of components.

16. A composition as claimed in any one of claims 1 to 15 wherein the sum of the fractional inhibitory concentration of the components is less than 0.7.

17. A composition as claimed in claim 16 wherein the sum of the fractional inhibitory concentration of the components is not more than 0.5.

18. A composition as claimed in any one of claims 1 to 17 which comprises a carrier and a composition of component (a) and one or both of the components (b)(i) and (b)(ii).

19. A medium which is susceptible to attack by micro-organisms and which contains from 0.0001 to 10% by weight of the medium of a composition as claimed in any one of claims 1 to 17.

20. A medium as claimed in claim 19 which is selected from a cooling water system, a paper mill liquor, a metal working fluid, a geological drilling lubricant, a polymer emulsion, a paint, a lacquer or a varnish.

21. A method for inhibiting the growth of micro-organisms on, or in, a medium, which comprises treating the medium with a composition as claimed in any one of claims 1 to 18.

22. A method as claimed in claim 21 wherein the medium which is treated is a cooling water system, a paper mill liquor, a metal working fluid, a geological drilling lubricant, a polymer emulsion, a paint, a lacquer, a varnish, leather or wood.

23. A composition which contains from 1 up to 1000 parts by weight of 1,2-benzisothiazolin-3-one and correspondingly from 1000 to 1 parts by weight of sodium 2-thiopyridine-1-oxide.

24. A composition which contains 1,2-benzisothiazolin-3-one, 2,2'-dithiopyridine-1,1'-dioxide and zinc chloride wherein 1,2-benzisothiazolin-3-one is present in an amount of from 1 to 1000 parts by weight and correspondingly the 2,2'-dithiopyridine-1,1'-dioxide and zinc chloride together are present in an amount of from 1000 to 1 parts by weight.

25. A composition as claimed in claim 1 and substantially as hereinbefore described with reference to the Examples.

DGJ/BH
22.3.89.

Published 1990 at The Patent Office, State House, 66 71 High Holborn, London WC1R 4TP. Further copies may be obtained from The Patent Office Sales Branch, St Mary Cray, Orpington, Kent BR5 3RD. Printed by Multiplex techniques ltd. St Mary Cray, Kent, Con. 1/87